

Su1
B4

What we claim is:

1. A method for stimulating angiogenesis within a targeted collection of viable cells in-situ, said method comprising the steps of:
 - identifying a collection of cells comprising viable cells in-situ as a target for stimulation of angiogenesis;
 - providing means for effecting an introduction of at least one member selected from the group consisting of the PR-39 oligopeptide collective to the cytoplasm of said targeted collection of cells;
 - introducing at least one member of the PR-39 oligopeptide collective to the cytoplasm of said targeted collection of cells using said effecting means;
 - allowing said introduced PR-39 oligopeptide collective member to interact with such proteasomes as are present within the cytoplasm of said targeted collection of cells whereby
 - (a) at least the α_7 subunit of the proteasomes interacts with said PR-39 oligopeptide collective member, and
 - (b) at least a part of the proteolytic activity mediated by proteasomes with an interacting α_7 subunit becomes selectively altered, and
 - (c) the selectively altered proteolytic activity of the proteasomes with an interacting α_7 subunit results in a stimulation of angiogenesis in-situ within the targeted collection of viable cells.

- 1000000000000000
2. A method for selective inhibition of proteasome-mediated degradation of peptides in-situ within a collection of viable cells, said method comprising the steps of:
identifying a collection of cells comprising viable cells in-situ as a target;
providing means for effecting an introduction of at least one member selected from the group consisting of the PR-39 oligopeptide collective to the cytoplasm of said targeted collection of cells;
introducing at least one member of the PR-39 oligopeptide collective to the cytoplasm of said targeted collection of cells using said effecting means;
allowing said introduced PR-39 oligopeptide collective member to interact with such proteasomes as are present within the cytoplasm of said targeted collection of cells whereby
(a) at least the α_7 subunit of the proteasomes interacts with the PR-39 oligopeptide collective member, and
(b) at least a part of the proteolytic activity mediated by proteasomes with an interacting α_7 subunit becomes markedly altered, and
(c) the markedly altered proteolytic activity of the proteasomes with an interacting α_7 subunit results in a selective inhibition of proteasome-mediated degradation of peptides in-situ within the targeted collection of cells.

3. The method as recited in claim 1 or 2 wherein said collection of viable cells includes at least one type of cell selected from the group consisting of endothelial cells,

myocytes and myoblasts, fibrocytes and fibroblasts, epithelial cells, osteocytes and osteoblasts, neuronal cells and glial cells, erythrocytes, leukocytes, and progenitor cells of all types.

4. The method as recited in claim 1 or 2 wherein said collection of cells comprises at least one tissue selected from the group consisting of myocardium, skeletal muscle, smooth muscle, an artery, a vein, lung, brain, kidney, spleen, liver, gastrointestinal tissue, nerve tissue, limbs, and extremities.

5. The method as recited in claim 1 or 2 wherein the means for an introduction of a PR-39 oligopeptide collective member include one selected from the group consisting of catheter-based introduction means, injection-based introduction means, infusion-based introduction means, localized intravascular introduction means, liposome-based introduction means, receptor-specific peptide introduction means, slow releasing means for peptide secretion in living cells and sequestered organisms.

6. The method as recited in claim 1 or 2 wherein the means for an introduction of a PR-39 oligopeptide collective member includes the DNA sequences coding for PR-39 oligopeptides of different sizes inserted in a suitable vector for transfection and subsequent expression of peptides within said cells.

7. The method as recited in claim 1 or 2 wherein said method is practiced under in-vivo conditions.

(D)

8. The method as recited in claim 1 or 2 wherein said method is practiced under in-vitro conditions.

B *C*

9. The method as recited in claim 1 or 2 wherein degradation of I κ B α is selectively inhibited.

B *A&C*

10. The method as recited in claim 1 or 2 wherein degradation of HIF-1 α is selectively inhibited.

Sub *B6*

11. A family of PR-39 derived oligopeptides whose members individually cause a selective inhibition of proteasome-mediated degradation of peptides in-situ after introduction intracellularly to a viable cell, each member of said oligopeptide family being:

a peptide less than 39 amino acid residues in length;

at least partially homologous with the N-terminal amino acid residue sequence of the native PR-39 peptide;

able to interact in-situ with at least the $\alpha 7$ subunit of such proteasomes as are present within the cytoplasm of the cell; and

able to alter markedly the proteolytic activity of proteasomes with an interacting $\alpha 7$ subunit such that a selective increased expression of specific peptides occurs in-situ.

B

12. The PR-39 derived oligopeptide family as recited in claim 11 whose membership includes a peptide comprised of 15 amino acid residues whose sequence is

Arg-Arg-Arg-Pro-Arg-Pro-Pro-Tyr-Leu-Pro-Arg-Pro-Arg-Pro-Pro. Seq 1D No 3

D6 C6

D6 C7

13. The PR-39 derived oligopeptide family as recited in claim 11 whose membership includes a peptide comprised of 11 amino acid residues whose sequence is

Arg-Arg-Arg-Pro-Arg-Pro-Pro-Tyr-Leu-Pro-Arg. Seq 1D No 4

D6 C8

14. The PR-39 derived oligopeptide family as recited in claim 11 whose membership includes a peptide comprised of 8 amino acid residues whose sequence is

Arg-Arg-Arg-Pro-Arg-Pro-Pro-Tyr. Seq 1D No 5

ADD
B7